REMARKS

This paper follows the filing of a Request for Continued Examination under 37 CFR § 1.114, and a Response to the previous Office Action. No Office Action has been issued since the RCE was filed. The changes shown above reflect amendments made from the claims as presented in the Response filed December 22, 2005.

Claims 41-62 and 65-82 are pending in this application and under examination. Claims 41-57 and 74-82 have been allowed, for which applicant is grateful. The other claims stand rejected for issues relating to practicing the claimed use of nucleic acid vectors expressing telomerase reverse transcriptase (TRT) *in vivo*.

Reconsideration of the application is respectfully requested.

Rejection under 35 USC § 112 ¶ 1

Claims 58-62 and 65-73 stand rejected as not being enabled by the specification for using TRT *in vivo*. The Office Action recommends that applicants consider limiting the claims to adenovirus, but rejects the Rudolph paper as a model for treating human disease since it uses gene knockout animals.

The rejected claims are amended in this response in accordance with what was discussed with Examiner Angell and Examiner Nguyen in the interview of this application at the Patent Office on December 13, 2005. Specifically, the claims now refer to *a method of reducing damage due to impaired replication of cells in a tissue or organ of a mammal in vivo*. Use of adenovirus is explicitly referred to in base claim 58. Particular target tissues of clinical and commercial interest are highlighted in dependent claims 63-74.

Applicants respectfully submit that the application as filed enables the skilled user to make and use an adenoviral vector encoding TRT for the purpose of reducing damage in a tissue or organ *in vivo*, in accordance with what is claimed. This has been confirmed using two different animal models for damage to two different tissues:

1. Data from a rabbit ear model (US 2004/0147465 A1) showed that increasing telomerase activity using an adenovirus *improves wound healing.*
2. Data from a mouse cirrhosis model (Rudolph et al., Science 287:1253-1257, 2000) showed that increasing telomerase activity using an adenovirus *makes the liver resistant to experimentally induced liver failure.*

Previous Declarations filed in this application under 37 CFR § 1.132 explain how the application as filed enables the skilled reader to make and use TRT vectors *in vivo,* and why the testing of this invention in animal models validates its use in humans:

1. The Declaration by Dr. John Irving, filed March 3, 2003, explains that the skilled reader would know from the specification how to make a TRT encoding adenovirus vector such as those subsequently used in the animal model experiments.
2. The Declaration by Dr. Calvin Harley, filed February 26, 2003, explains that adenovirus vectors made according to the specification have been tested in several models to confirm the ability of these vectors to extend replicative capacity of cells, both *in vitro* and *in vivo.*
3. The Declaration by Dr. Edward Wirth, filed December 24, 2004, explains that the mouse cirrhosis experiments described in the Rudolph paper provide a good model for the use of TRT to extend replicative capacity of liver cells in human subjects.

Accompanying the present Amendment is a second § 1.132 Declaration by Dr. Calvin Harley, Chief Scientific Officer of Geron Corporation. Also enclosed is a review article by Dr. Harley published recently in Current Molecular Medicine (vol. 5:29-38, 2005). The article discusses evidence from Geron Corporation and elsewhere that telomerase activation has important potential as therapeutic agents in the treatment of degenerative diseases.

Dr. Harley explains in his Declaration that adenovirus vectors are suitable for transducing a variety of tissue types *in vivo*, thereby increasing telomerase enzyme activity and improving replicative capacity of the cells. He says that in clinical conditions where there is damage due to impaired cell replication, treatment with a TRT expression vector can increase the speed or extent of replication, or otherwise confer benefits to reduce damage or promote healing.

Dr. Harley also elaborates on particular tissues and disease conditions that are expected to benefit from gene therapy using TRT. These include conditions of the skin, hair, hepatocytes,

endothelial cells, RPE cells, cementoblasts, odontoblasts, osteoblasts, chondrocytes, stromal cells, mesenchymal stem cells, cardiomyocytes, and leukocytes.

Thus, the effectiveness of TRT vectors for treating degenerative diseases or reducing damage in a tissue or organ *in vivo* has been confirmed in several animal models. From what is described in the specification, the skilled reader will be able to use TRT vectors for reducing damage in other tissues, both in animal models and (in the normal course of clinical trials) in human subjects.

Withdrawal of this rejection is respectfully requested.

Previous Information Disclosure Statement

Applicants note that the form PTO-1449 from the Information Disclosure Statement filed December 27, 2001, was not initialed by Examiner Ramirez, who was responsible for this application at that time.

Applicants respectfully request that the current Examiner acknowledge consideration of the information enclosed therewith by initialing the corresponding PTO-1449, another copy of which is enclosed herewith for convenience.

Supplemental Information Disclosure Statement

Being filed under separate cover is a new supplemental IDS, providing PCT patent applications and published articles referred to in Dr. Harley's Declaration, and other information that may be helpful in examination of this application.

The Examiner is reminded under 37 CFR § 1.56 that there are other patents and applications pending that relate to telomerase. These include the patents and applications listed in the Appendix that follows. Recent developments include issuance of U.S. Patents 6,921,664, 6,927,285, and 7,005,262, and allowance of USSN 09/843,676.

Request for Interview

Applicants respectfully request that all outstanding rejections be reconsidered and withdrawed. The application is believed to be in condition for allowance, and a prompt Notice of Allowance is requested.

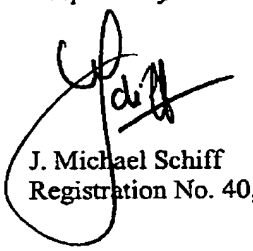
In the event that the Examiner determines that there are other matters to be addressed, the undersigned hereby requests a further interview by telephone.

Fees

No fee is believed payable with respect to the filing of this paper, since there has been no Office Action since the Request for Continued Examination was filed on December 20, 2005.

However, should the Patent Office determine that an extension of time or any other relief is required for further consideration of this application, applicants hereby petition for such relief, and authorize the Commissioner to charge the cost of such petitions and other fees due in connection with the filing of these papers to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,



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APPENDIX

Other patents and applications

Recombinant hTRT	U.S. Patent 6,475,789; U.S. Patent 6,261,836; U.S. Patent 6,617,110; U.S. Patent 6,808,880; U.S. Patent 6,921,664; U.S. Patent 6,927,285; U.S. Patent 7,005,262; USSN 09/843,676 (allowed); USSN 08/974,584; USSN 09/432,503; USSN 09/721,477; USSN 09/721,506; USSN 10/053,758; USSN 10/044,692; USSN 10/877,022; USSN 10/877,124; USSN 10/044,539; USSN 10/877,146; USSN 11/207,078 (all pending)
hTRT variants	U.S. Patent 6,337,200; USSN 09/990,080
TRT from single cell ciliates	U.S. Patent 6,093,809; U.S. Patent 6,166,178; U.S. Patent 6,309,867
Mouse TRT	U.S. Patent 6,767,719; USSN 10/862,698
Telomerase holoenzyme purified from cells having telomerase activity	U.S. Patent 5,968,506; U.S. Patent 6,261,556; U.S. Patent 6,517,834; U.S. Patent 6,545,133; U.S. Patent 6,787,133; USSN 10/811,033
Use of recombinant hTRT in vaccine formulations	U.S. Patent 6,440,735; USSN 10/208,243; USSN 10/602,441
hTRT promoter	U.S. Patent 6,610,839; U.S. Patent 6,777,203; USSN 10/325,810; USSN 10/674,836
hTRT antisense oligonucleotides	U.S. Patent 6,444,650; U.S. Patent 6,627,619; USSN 10/637,443